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Nielsen, Line Hagner; Keller, Stephan Sylvest; Jacobsen, J.; Boisen, Anja; Müllertz, A.

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In vitro characterization of microcontainers as an oral drug delivery system

Hagner Nielsen L.[1]; Sylvest Keller S.[2]; Jacobsen J.[1]; Boisen A.[2]; Müllertz A.[1,3]
[3]Bioneer:FARMA, [1]Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, 2100 Copenhagen, Denmark
[2]Department of Micro and Nanotechnology, Technical University of Denmark, 2800 Kongens Lyngby, Denmark

Introduction: Micro fabricated drug delivery devices have been proposed as an approach for delivering drugs orally as they can protect the drug through the stomach and thereby, possibly improve the oral bioavailability [1,2]. Microcontainers are polymeric devices consisting of a flat base with a walled reservoir (Figure 1) [2,3], and as only one side of the microcontainers is open, they allow for unidirectional release of the drug directly to the intestinal mucosa.
The purpose of this study was to investigate the microcontainers as an innovative oral drug delivery system for the poorly water-soluble drug, furosemide.
Method: Microcontainers, with an inner diameter of 223 µm (Figure 1), were fabricated through two steps of photolithography defining the bottom and the walls of the microcontainers. The microcontainers were filled with amorphous furosemide sodium salt (prepared by spray drying). Subsequently, a 7 µm layer of Eudragit L100 (Evonik Industries, Essen Germany) was spray coated (ExactaCoat, Sono-Tek, USA) on the cavity of the drug-filled microcontainers. The release of the drug from the microcontainers was evaluated in a biorelevant gastric medium at pH 2 and a biorelevant intestinal medium at pH 6.5. The intestinal permeability of the amorphous furosemide salt loaded into the microcontainers was evaluated using the Caco-2 cell model with biorelevant intestinal medium pH 6.5 as the apical medium.
Results: From the release experiments, it was observed that the Eudragit layer prevented drug release in gastric medium, while an immediate release of the amorphous furosemide salt was seen in the intestinal medium. The permeability studies showed a fast absorption of the amorphous furosemide salt with no significant difference between the microcontainers (P_{app} $1.79 \cdot 10^{-5} \pm 0.68 \cdot 10^{-6}$ cm/s, mean±SD n=11) and bulk powder of amorphous furosemide salt (P_{app} $1.62 \cdot 10^{-5} \pm 1.039 \cdot 10^{-5}$ cm/s, mean±SD n=11) (Figure 2).
Conclusion: Microcontainers were successfully fabricated and loaded with powder drug. The Eudragit layer prevented drug release in gastric medium, and facilitated an immediate release in the intestinal medium. Furthermore, the amorphous furosemide salt loaded in microcontainers was fast absorbed through the Caco-2 cell monolayer. Microcontainers therefore show considerable future potential as oral drug delivery systems.

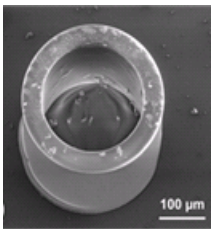

Figure 1: SEM image of a microcontainer with an inner diameter of 223 µm.

Figure 2: The intestinal permeability through Caco-2 cells of the amorphous furosemide salt in bulk form and loaded into microcontainers

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